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64) Hair-growing agent.

57) A hair-growing agent which exhibits a strong hair-growing effect. The hair-growing agent according to the present invention contains as an effective ingredient an aliphatic carboxylic acid having an odd number of carbon atoms or a derivative thereof.

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Hair-growing agent

The present invention relates to a hair-growing agent.

Hair-growing agents containing various agents exhibiting pharmaceutical properties are known. Such pharmaceutical agents may include, for example, a
5 vitamin such as vitamin E, an amino acid such as serine or methionine, a vasodilator such as an acetylcholine derivative, an anti-inflammatory agent such as lithospermum root extract, a female sex hormone such
10 as estradiol, a skin function stimulant such as cepharanthine, a melanine synthesis catalyst such as copper pantothenate, a keratolytic such as salicylic acid, or the like. These agents may assist in the prevention and cure of alopecia.

15 There are known cases where an aliphatic carboxylic acid or a derivative thereof such as natural vegetable oil, e.g., olive oil and castor oil, or stearic acid is contained in a hair cosmetic such as a hair tonic or the like to improve performance of the product. Aliphatic
20 carboxylic acids constituting various naturally occurring lipids, such as vegetable oils and animal oils, are in almost all cases aliphatic carboxylic acids having an even number of carbon atoms, whether they are saturated aliphatic carboxylic acids such as stearic acid and
25 palmitic acid or unsaturated aliphatic carboxylic acids

such as oleic acid and linoleic acid. There are no known cases where an aliphatic carboxylic acid having an odd number of carbon atoms or a derivative thereof is used in a hair cosmetic.

5 Conventional hair-growing agents are claimed to be effective in preventing or improving dandruff, itchiness and hair loss as well as in accelerating hair generation and growth. However, it seems that a satisfactory effect has not yet been obtained.

10 Therefore, the object of the present invention is to provide a hair-growing agent exhibiting a strong hair-growing effect.

15 The object can be accomplished by providing a hair-growing agent comprising as an effective ingredient an aliphatic carboxylic acid having an odd number of carbon atoms or a derivative thereof.

 The hair-growing agent according to the present invention provides a strong hair-growing effect.

20 Alopecia may arise from various causes. In each case, individual hairs cannot complete their normal hair cycle to reach the telogen state. In order to decrease baldness and accelerate hair generation, it is necessary to bring the hair follicles from the telogen state into the normal anagen state. As a result of extensive
25 research into the conversion of hair from the telogen state into the anagen state, it has been found that an aliphatic carboxylic acid having an odd number of carbon atoms and a derivative thereof exhibit a remarkable hair-growing effect. The present invention is based on
30 this finding.

 The aliphatic carboxylic acid to be used for the hair-growing agent according to the present invention may be a saturated or unsaturated aliphatic carboxylic acid provided it has an odd number of carbon atoms.
35 The unsaturated aliphatic carboxylic acid may contain a plurality of double bonds. The aliphatic carboxylic acid may be a lower aliphatic carboxylic acid such as

propionic acid (having 3 carbon atoms) or valeric acid (having 5 carbon atoms), or a higher aliphatic carboxylic acid such as tricosanoic acid (having 23 carbon atoms) or pentacosanoic acid (having 25 carbon atoms).

5 Preferred aliphatic carboxylic acids having an odd number of carbon atoms may include propionic acid, valeric acid, heptanoic acid, nonanoic acid, undecanoic acid, tridecanoic acid, pentadecanoic acid, heptadecanoic acid, nonadecanoic acid, heneicosanoic acid, tricosanoic acid
10 and pentacosanoic acid.

For the hair-growing agent according to the present invention, any derivative of an aliphatic carboxylic acid having an odd number of carbon atoms as enumerated hereinabove may be used as an effective ingredient.

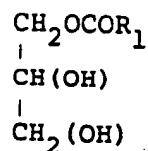
15 However, needless to say, any compound which may adversely affect the human body cannot be used.

Preferred derivatives include the following.

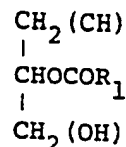
A) a monoglyceride represented by the general formula (I) or (II):

20

(I)



(II)



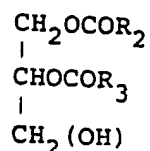
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where R_1 is a straight-chain aliphatic group having an even number of carbon atoms.

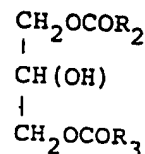
B) a diglyceride represented by the general formula (III) or (IV):

30

(III)



(IV)



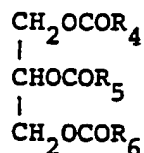
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where at least one of R_2 and R_3 is a straight-chain aliphatic group having an even number of carbon atoms.

It should be noted here that the effect to be accomplished by the present invention can be achieved if either R_2 or R_3 represents an aliphatic group having an even number of carbon atoms while the other represents a hydrogen or an aliphatic group having an odd number of carbon atoms or another organic group which does not adversely affect the human body. However, a diglyceride of an aliphatic carboxylic acid having an odd number of carbon atoms is particularly preferred.

C) a triglyceride represented by the general formula (V):

(V)



where at least one of R_4 , R_5 and R_6 is a straight-chain aliphatic group having an even number of carbon atoms.

It should be noted here that, where at least one of R_4 , R_5 and R_6 is a aliphatic group having an even number of carbon atoms, the effect sought by the present invention can be achieved even if the others are in each case hydrogen or an aliphatic group having an odd number of carbon atoms or another organic group which does not adversely affect the human body. However, a triglyceride of an aliphatic carboxylic acid having an odd number of carbon atoms is particularly preferred.

D) an aliphatic carboxylic acid salt represented by the general formula (VI):

(VI)



where R_7 is a straight-chain aliphatic group having an even number of carbon atoms, M is a metal atom, and n is an integer corresponding the valence of M. Representatives may be $R_7\text{COONa}$, $R_7\text{COOK}$ and $R_7\text{COOLi}$.

E) an ester represented by the general formula (VII):

(VII)

5



where R_8 is a straight-chain aliphatic group having an even number of carbon atoms, R_9 is a residue of a primary or secondary alcohol, an amine residue, a polyoxyethylene residue, a sorbitan residue or a sucrose residue. A representative primary alcohol may be methanol and ethanol, and a representative amine residue is mono-, di- and tri-ethanolamine.

10 F) a primary amide represented by the general formula (VIII):

15

(VIII)

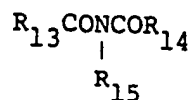


where R_{10} is a straight-chain aliphatic group having an even number of carbon atoms, and R_{11} and R_{12} are independently a hydrogen atom or an organic group having no adverse effect on the human body.

20 G) a secondary amide represented by the general formula (IX):

25

(IX)



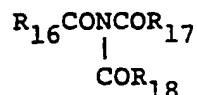
where at least one of R_{13} and R_{14} is a straight-chain aliphatic group having an even number of carbon atoms, and R_{15} may be a hydrogen atom or any organic group which does not adversely affect the human body. It should be noted here that where at least one of R_{13} and R_{14} is an aliphatic group having an even number of carbon atoms the effect of the present invention can be achieved, and that the other may be any organic group which does not adversely affect the human body although it is particularly preferred that both be

a straight-chain aliphatic group having an even number of carbon atoms.

H) a tertiary amide represented by the general formula (X):

5

(X)



10

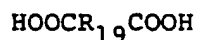
where at least one of R_{16} , R_{17} and R_{18} is a straight-chain aliphatic group having an even number of carbon atoms. It is to be noted that where at least one of R_{16} , R_{17} and R_{18} is an organic group with an even number of carbon atoms, the present invention can achieve the desired effect, and also that the others may each be any organic group exerting no adverse influence on the human body. However, it is particularly preferred that all three be independently a straight-chain aliphatic group having an even number of carbon atoms.

15

I) a dibasic carboxylic acid represented by the general formula (XI) or a salt thereof:

20

(XI)



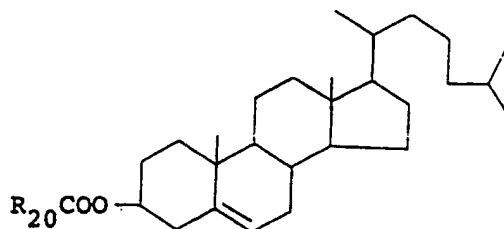
25

where R_{19} is a straight-chain aliphatic group having an odd number of carbon atoms.

J) a sterol ester represented by the general formula (XII):

(XII)

30

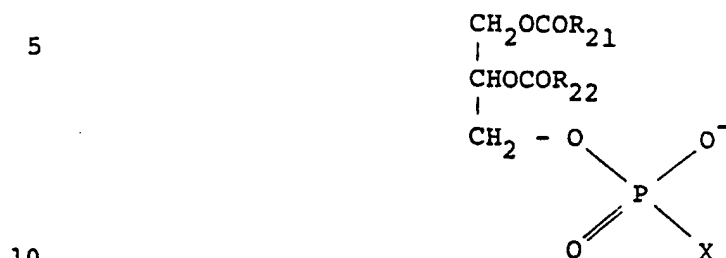


35

where R_{20} is a straight-chain aliphatic group having an even number of carbon atoms.

K) a phospholipid represented by the general formula (XIII):

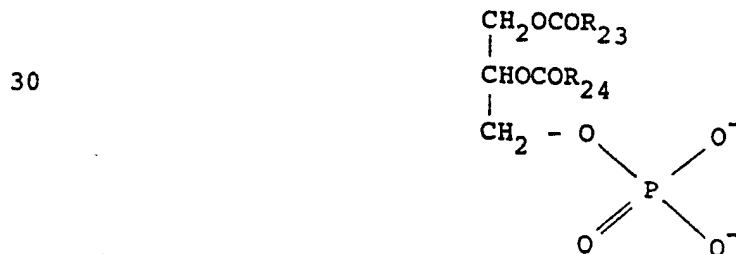
(XIII)



where at least one of R_{21} and R_{22} is an straight-chain aliphatic group having an even number of carbon atoms, and the other may be a hydrogen or an organic group having no adverse effect on the human body. However, it is preferred that both of R_{21} and R_{22} are independently a straight-chain aliphatic group having an even number of carbon atoms. X is a choline residue, an ethanolamine residue, a serine residue or an inositol residue. When X is a choline residue, it represents a phosphatidyl choline. When X is a ethanolamine residue, it represents a phosphatidyl ethanolamine. When X is a serine residue, it represents a phosphatidyl serine. When X is a inositol residue, it represents a phosphatidyl inositol.

L) a phosphatidic acid represented by the general formula (XIV):

(XIV)

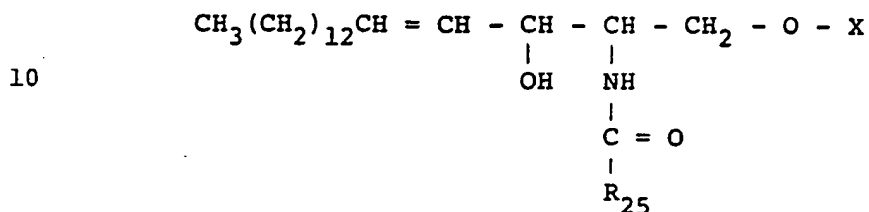


where at least one of R_{23} and R_{24} is an straight-chain aliphatic group having an even number of carbon atoms, and the other is a hydrogen or an organic group having

no adverse effect on the human body. However, it is preferred that both of R_{23} and R_{24} are independently a straight-chain aliphatic group having an even number of carbon atoms.

5 M) a sphingolipid represented by the general formula (XV):

(XV)



15 where R_{25} is a straight-chain aliphatic group having an even number of carbon atoms, and X is a sugar residue, a phosphate residue or an amine base residue such as choline or ethanolamine.

20 The hair-growing agent according to the present invention may be used in a conventional manner in a variety of forms such as a hair-growing agent for an endermic liniment, a hair-growing agent for internal use, a hair-growing agent to be taken by injection, a hair tonic, hair lotion, hair cream, hair shampoo, hair rinse or the like.

25 In addition to the above-mentioned effective ingredients, the hair-growing agent according to the present invention may usually contain a cosmetically or pharmaceutically acceptable carrier. Such a carrier is not described in detail here since it is well known in
30 this field. Examples of such a carrier include water; ethanol; a polyol such as ethylene glycol, propylene glycol, 1,3-butylene glycol, glycerine or sorbitol; a siloxane such as dimethyl polysiloxane, phenyl polysiloxane or polyoxyalkylene polysiloxane; an animal
35 or vegetable oil such as sperm oil or jojoba oil; liquid paraffin; vaseline; paraffin wax; squalane; and an olefin oligomer.

The hair-growing agent according to the present invention may also contain an effective ingredient that is conventionally used. Such an effective ingredient may include, for example, a vitamin such as vitamin E, a hormone such as estradiol, a vasodilator such as an acetylcholine derivative, an amino acid such as serine or methionine, an anti-inflammatory agent such as lithospermum root extract, a skin function stimulant such as cepharanthine, or a keratolytic such as salicylic acid.

Test 1: Animal Study for Evaluating Effectiveness

Aliphatic carboxylic acids having an odd number of carbon atoms and derivatives thereof were tested for their hair growing effects.

The tested substances were linear saturated aliphatic carboxylic acids having carbon atoms in variously odd and even numbers, and triglycerides of the aliphatic carboxylic acids. Test specimens were prepared by dissolving each test substance to be tested in ethanol. Concentrations of the test substance were 0.3, 3.0 and 10.0% by weight, respectively. As a control, ethanol containing no test substance was also tested.

The test animals were groups of 6 to 8 male rabbits of New Zealand White species each weighing about 2.5 kg from whose backs hair was removed. Rabbits in the telogen state alone were used. The test specimen was applied in the amount of 0.2 ml twice per week for 30 to 60 days to the area of the rabbits' backs from which the hair had been removed. The test was conducted by observing the number of days required for the conversion of hair from the telogen state into the anagen state. The results are shown in Table 1 below. In the Table, "shortened days" means the number of days by which the conversion of the telogen state into anagen state is shortened, compared with the control in which ethanol containing no test substance was applied. For example,

when the number of shortened days is 10, it means that the conversion of telogen state into anagen state occurred 10 days earlier than the control experiment.

Table 1

Test substance	Concentration (% by weight)	Hair-growing effect	
		Shortened days	Overall evaluation
Propionic acid	0.3	10	Effective
Valeric acid	0.3	12	Effective
Heptanoic acid	0.3	12	Effective
Nonanoic acid	0.3	14	Effective
Hendecanoic acid	0.3	18	Effective
Tridecanoic acid	0.3	20	Effective
Pentadecanoic acid	0.3	22	Effective
Heptadecanoic acid	0.3	22	Effective
Nonadecanoic acid	0.3	16	Effective
Heneicosanoic acid	0.3	12	Effective
Tricosanoic acid	0.3	12	Effective
Pentacosanoic acid	0.3	12	Effective
Butyric acid	0.3	2	Ineffective
Caproic acid	0.3	1	Ineffective
Caprylic acid	0.3	3	Ineffective
Capric acid	0.3	3	Ineffective
Lauric acid	0.3	1	Ineffective
Myristic acid	0.3	0	Ineffective
Palmitic acid	0.3	0	Ineffective
Stearic acid	0.3	0	Ineffective
Arachic acid	0.3	0	Ineffective
Behenic acid	0.3	0	Ineffective
Lignoceric acid	0.3	0	Ineffective

Test substance	Concentration (% by weight)	Hair-growing effect	
		Shortened days	Overall evaluation
Tripropionin	3.0	10	Effective
Tripentanoin	3.0	16	Effective
Triheptanoin	3.0	20	Effective
Trinonanoin	3.0	22	Effective
Trihendecanoin	3.0	26	Remarkably effective
Tritridecanoin	3.0	28	Remarkably effective
Tripentadecanoin	3.0	30	Remarkably effective
Triheptadecanoin	3.0	30	Remarkably effective
Trinonadecanoin	3.0	22	Effective
Triheneicosanoin	3.0	18	Effective
Tritricosanoin	3.0	16	Effective
Tributyryn	3.0	2	Ineffective
Tricaprone	3.0	2	Ineffective
Tricaprin	3.0	4	Ineffective
Tricaprylin	3.0	2	Ineffective
Trilaurin	3.0	0	Ineffective
Trimyristin	3.0	0	Ineffective
Tristearin	3.0	0	Ineffective
Triarachin	3.0	0	Ineffective
Tribehen	3.0	0	Ineffective
Trilignocerin	3.0	0	Ineffective

Test substance	Concentration (% by weight)	Hair-growing effect	
		Shortened days	Overall evaluation
Tripropionin	10.0	12	Effective
Tripentanoin	10.0	16	Effective
Triheptanoin	10.0	20	Effective
Trinonanoin	10.0	24	Effective
Trihendecanoin	10.0	28	Remarkably effective
Tritridecanoin	10.0	28	Remarkably effective
Tripentadecanoin	10.0	32	Remarkably effective
Triheptadecanoin	10.0	32	Remarkably effective
Trinonadecanoin	10.0	24	Effective
Triheneicosanoin	10.0	18	Effective
Tritricosanoin	10.0	18	Effective
Tributyryn	10.0	3	Ineffective
Tricaprone	10.0	2	Ineffective
Tricaprin	10.0	4	Ineffective
Tricaprylin	10.0	4	Ineffective
Trilaurin	10.0	2	Ineffective
Trimyristin	10.0	0	Ineffective
Tripalmitin	10.0	0	Ineffective
Tristearin	10.0	0	Ineffective
Triarachin	10.0	0	Ineffective
Tribehen	10.0	0	Ineffective
Trilignocerin	10.0	0	Ineffective

It can be seen from Table 1 that the aliphatic carboxylic acids having an odd number of carbon atoms and the glycerides thereof have significant hair-growing effects whereas the aliphatic carboxylic acids having even-numbered carbon chains as long as the former and the glycerides thereof have no hair-growing effect.

Test 2: Human Study for Evaluating Effectiveness

A hair-growing composition comprising 10.0% by weight of n-trihendecanoin, 1.0% by weight of castor oil, 0.5% by weight of pyrrolidone carboxylic acid, 0.5% by weight of a perfume and 88% by weight of 80% ethanol was prepared. This composition was then used by patients (totaling 25 patients) suffering from various types of alopecia over a period of 3 to 6 months. The effects were evaluated according to subjective observation by the patients themselves. The results are shown in Table 2 below.

Table 2

Alopecia	No. of cases	Results		
		Remarkably Effective	Effective	Ineffective
Alopecia areata	9	3	3	3
Alopecia praematura and praesenilis	10	3	4	3
Alopecia furfuracea	3	0	2	1
Alopecia seborrheica	3	1	0	2

It can be seen from Table 2 that the hair-growing agent according to the present invention is effective for various types of alopecia, particularly for male alopecia such as alopecia praematura and alopecia praesenilis as well as alopecia areata.

Test 3: Human Study for Evaluating Safety

Pieces of gauze of 1 cm in diameter were soaked with the hair-growing composition prepared for Test 2. As a control, pieces of gauze of 1 cm in diameter were soaked with water.

Two pieces of each type of gauze (totaling 4 pieces) were attached as a closed patch by means of a fin chamber to the antebrachial flexor side of 25 healthy females for 24 hours. The skin conditions were observed after 30 minutes and 24 hours of the removal of the gauze. The result was that none of the women had any skin irritation.

The following indicates forms and compositions as examples of the hair-growing agents according to the present invention. In the following, the compositions are expressed in terms of % by weight.

Example 1

Hair-Growing Composition for Endermic Liniment

	Ingredient	Amount
20	80% ethanol	88
	n-trihendecanoic	10.0
	Castor oil	1.0
	Pyrrolidone carboxylic acid	0.5
	Perfume	0.5

25 Example 2

Hair-Growing Composition for Endermic Liniment

	Ingredient	Amount
	85% ethanol	97.5
	n-nonanoic acid	0.5
30	Olive oil	1.0
	α -tocopherol	0.5
	Perfume	0.5

Example 3

Hair-Growing Composition for Endermic Liniment

	Ingredient	Amount
35	90% ethanol	92.5
	n-tritridecanoic	5.0

Olive oil	1.0
Glycyrrhizin	1.0
Perfume	0.5

Example 4

5 Hair-Growing Composition for Endermic Liniment

	Ingredient	Amount
	90% ethanol	89.5
	Ethyl n-tridecanoate	3.0
	Liquid paraffin	5.0
10	Polyethylene glycol	2.0
	Perfume	0.5

Example 5

Shampoo Composition

	Ingredient	Amount
15	Lauryl ether sodium sulfate	5.0
	α -olefin sodium sulfonate	10.0
	Lauryl sulfate triethanol amine	5.0
	n-tritridecanoin	3.0
	Purified water	77.0

20 Example 6

Hair Rinse Composition

	Ingredient	Amount
	Stearyl trimethyl ammonium chloride	1.5
25	Distearyl dimethyl ammonium chloride	0.5
	Cetanol	1.5
	Polyoxyethylene stearyl ether ($\bar{P}=5$)	2.0
	Liquid paraffin	1.0
30	Trihendecanoin	3.0
	Purified water	90.5

Example 7

Hair Cream Composition

	Ingredient	Amount
35	n-tripentadecanoin	10.0
	Olive oil	5.0
	Liquid paraffin	51.0

Beeswax	1.0
Sorbitan sesquioleate	3.0
Purified water	30.0

Example 8

5 Hair Tonic Composition

Ingredient	Amount
Ethyl n-nonanoate	3.0
Chillies tincture	0.5
Hinokitiol	0.1
10 α -tocopherol	0.3
Castor oil	10.0
Ethanol	86.1

Example 9

Hair-Growing Composition for Internal Use

Ingredient	Amount
15 n-tripentadecanoin	68.0
Lactose	20.0
Corn starch	10.0
Magnesium stearate	2.0

20 Example 10

Hair-Growing Composition to be taken by Injection

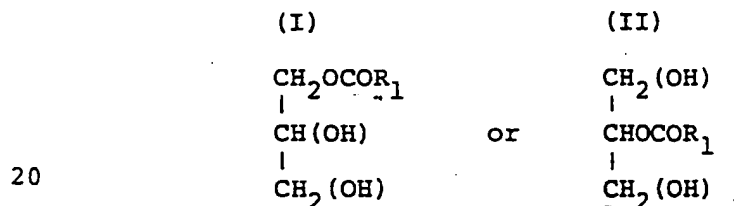
Ingredient	Amount
Tritridecanoin	0.5
Olive oil	99.5

Claims:

1. A hair-growing agent comprising an aliphatic carboxylic acid having an odd number of carbon atoms
5 or a derivative thereof as an effective ingredient.

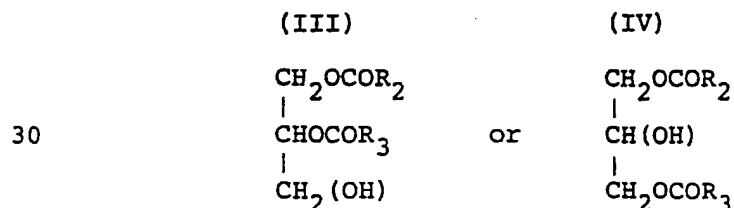
2. The hair-growing agent according to claim 1 wherein the effective ingredient is n-propionic acid, n-valeric acid, n-heptanoic acid, n-nonanoic acid, n-hendecanoic acid, n-tridecanoic acid, n-pentadecanoic
10 acid, n-heptadecanoic acid, n-nonadecanoic acid, n-heneicosanoic acid, n-tricosanoic acid, n-pentacosanoic acid or a triglyceride thereof.

3. The hair-growing agent according to claim 1 wherein said derivative is a monoglyceride represented
15 by the general formula:



where R_1 is a straight-chain aliphatic group having an even number of carbon atoms.

4. The hair-growing agent according to claim 1 wherein said derivative is a diglyceride represented by
25 the general formula:



where R_2 and R_3 are independently a hydrogen atom or an organic group, at least one thereof being a straight-
35 chain aliphatic group having an even number of carbon atoms.

5. The hair-growing agent according to claim 1

wherein said derivative is a triglyceride represented by the general formula:

(V)



where R_4 , R_5 and R_6 are independently a hydrogen atom or an organic group, at least one thereof being a straight-chain aliphatic group having an even number of carbon atoms.

6. The hair-growing agent according to claim 1 wherein said derivative is an aliphatic carboxylic acid salt represented by the general formula:

(VI)



where R_7 is a straight-chain aliphatic group having an even number of carbon atoms, M is a metal atom, and n is an integer corresponding to the valence of M.

7. The hair-growing agent according to claim 1 wherein said derivative is an ester represented by the general formula:

(VII)



where R_8 is a straight-chain aliphatic group having an even number of carbon atoms, R_9 is a residue of a primary or secondary alcohol, an amine residue, a polyoxyethylene residue, a sorbitan residue or a sucrose residue.

8. The hair-growing agent according to claim 1 wherein said derivative is a primary amide represented by the general formula:

(VIII)



where R_{10} is a straight-chain aliphatic group having an even number of carbon atoms, and R_{11} and R_{12} are independently a hydrogen atom or an organic group.

- 5 9. The hair-growing agent according to claim 1 wherein said derivative is a secondary amide represented by the general formula:

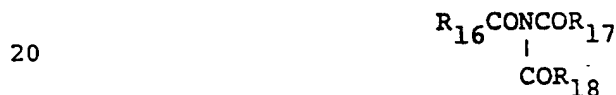
(IX)



where R_{13} and R_{14} are independently an organic group, at least one thereof being a straight-chain aliphatic carboxylic acid having an even number of carbon atoms, and R_{15} is a hydrogen atom or an organic group.

- 15 10. The hair-growing agent according to claim 1 wherein said derivative is a tertiary amide represented by the general formula:

(X)



where R_{16} , R_{17} and R_{18} are independently an organic group, at least one thereof being a straight-chain aliphatic group having an even number of carbon atoms.

- 25 11. The hair-growing agent according to claim 1 wherein said derivative is a dibasic carboxylic acid represented by the general formula (XI) or a salt thereof, wherein the general formula (XI) is:

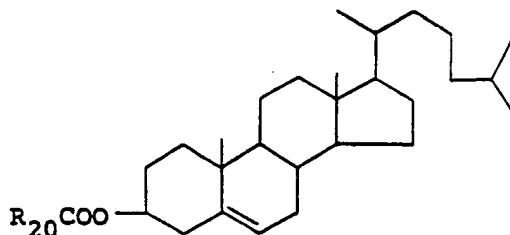
(XI)



where R_{19} is a straight-chain aliphatic group having an odd number of carbon atoms.

- 35 12. The hair-growing agent according to claim 1 wherein said derivative is a sterol represented by the general formula:

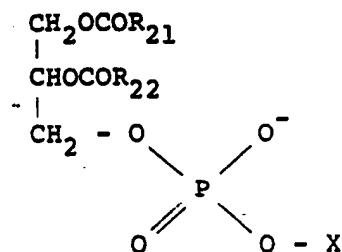
(XII)



10 where R_{20} is a straight-chain aliphatic group having an even number of carbon atoms.

13. The hair-growing agent according to claim 1 wherein said derivative is a phospholipid represented by the general formula:

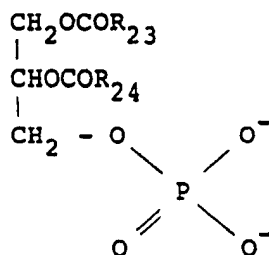
(XIII)



25 where R_{21} and R_{22} are independently a hydrogen atom or an organic group, at least one thereof being a straight-chain aliphatic group having an even number of carbon atoms, and X is a choline residue, an ethanolamine residue, a serine residue or an inositol residue.

14. The hair-growing agent according to claim 1 wherein said derivative is a phosphatidic acid represented by the general formula:

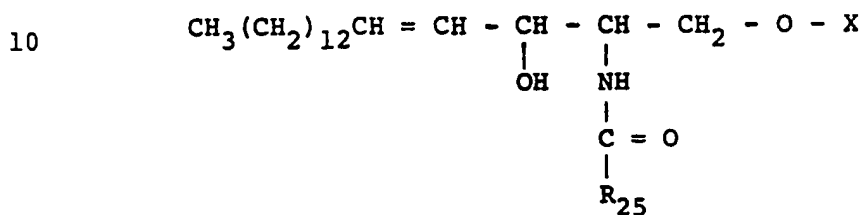
(XIV)



where R_{23} and R_{24} are independently a hydrogen atom or an organic acid, at least one thereof being a straight-chain aliphatic group having an even number of carbon atoms.

- 5 15. The hair-growing agent according to claim 1 wherein said derivative is a sphingolipid represented by the general formula:

(XV)



- 15 where R_{25} is a straight-chain aliphatic group having an even number of carbon atoms, and X is a sugar residue, a phosphate residue or an amine salt residue.